## REMARKS

Claims 1-3 and 7-11 are canceled. Claims 4-6 and 12-14 are pending in the instant application. Claim 4 has been amended to be directed to a method of making mineralized nanofibers comprising preparing a first solution with at least one peptide amphiphile comprising a $C_6$ or greater hydrocarbon component and a lyophilic peptide component, wherein the peptide amphiphile has a net ionic charge and at least one ion of a mineral salt, wherein the ion of the mineral salt has the same signed net ionic charge as the peptide-amphiphile; preparing a second solution with ion of a mineral salt having an opposite signed ionic charge to the net ionic charge of the peptide-amphiphile of said first solution; and mixing said first and second solutions to self-assemble said peptide amphiphiles into nanofibers and a nanofiber gel, wherein minerals nucleate at the nanofibers surfaces, wherein said nanofibers are fibrous cylindrical micelles. Claim 5 has been amended to delete "material" and insert therefore "mineral."

The amendment defining the peptide amphiphile as comprising a $C_6$ or greater hydrocarbon component and a lyophilic peptide component is supported, e.g., in paragraphs [0023] and [0032]. The amendment defining the net ionic charge of the peptide amphiphile is found, e.g., in Table 2. Finally, the amendment to the claim defining nanofibers as fibrous cylindrical micelles is supported, e.g., in paragraph [0035]. Accordingly, no new matter is added by these amendments. Applicants request entry of these amendments.

*Continuing Data and Priority*

The Office Action states that U.S. Provisional Appln. No. 60/425,536 does not provide adequate support for the claimed invention of claims 4-6 of the instant application. It concludes that this application is not accorded priority.

To clarify, Applicants respectfully submit that this application is based on provisional applications, Appln. Nos. 60/425,689 and 60/425,536, both of which were filed on November 12, 2002. To the extent that Appln. No. 60/425,536 does not provide support for claims 4-6, Applicants respectfully submit that Appln. No. 60/425,689 does

provide such support. As such, Applicants respectfully submit that this application is still accorded the benefit to the filing date of November 12, 2002.

*35 USC 112, First Paragraph*

Claims 4-6 and 12-14 are rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement. It is stated that the limitation of "minerals nucleate at the nanofiber surface," as amended into claim 4 on 21 August 2007, is not supported in the specification as originally filed. Applicants respectfully disagree.

This language is supported throughout the specification. For example, original claim 9 recites a " composition comprising: a material nucleated and grown on the surface of nanofibers in a nanofiber gel; said material grown and oriented on the surfaces of said fibers substantially throughout the nanofiber gel." (Original claim 9; emphasis added.) Furthermore, the abstract clearly states that: "[t]emplated mineralization of the initially dissolved mineral cations and anions in the mixture occurs with preferential orientation of the mineral crystals along the fiber surfaces within the nanofiber gel." (Abstract.) Therefore, the limitation, "minerals nucleate at the nanofiber surface," is clearly supported and withdrawal of the rejection is respectfully requested.

*35 USC 112, Second Paragraph*

Claims 4 and 6 remain, and claims 5 and 12-14 are rejected under 35 USC 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention.

The rejection iterates that the language "one ionically charged species of peptide amphiphile" is unclear because the claim does not make it clear as to (i) whether or not the species is homogeneous and (ii) whether or not "ionically charged species" refers to net negatively or positively charged molecules. Applicants have amended the claims to refer to the net charge of the peptide-amphiphile molecules. Support for this amendment is found in the specification, for example, in Table 2.

Furthermore, Applicants respectfully contend that whether or not the first solution contains a homogenous set of peptide amphiphiles does not render the claim unclear. In fact, it is contemplated in the specification that there can be one or more peptide amphiphiles, so long as the peptide amphiphiles have the same signed charge. For example, paragraph [0030] provides that "[i]n another embodiment, the compositions can further comprise mixture of peptide-amphiphiles having the same signed ionic charge, but having different peptide sequences, functional groups, or magnitude of ionic charge." (Specification at para. [0030]). Nevertheless, Applicants have clarified the claim language to recite that the first solution comprises at least one peptide amphiphile having a net ionic charge.

Finally, Applicants have amended claim 5 to correct its antecedent basis for the term "mineral," which is clearly recited in independent claim 1.

In view of the foregoing amendments, withdrawal of the rejections is proper.

*35 USC 102 – Wong et al.*

Claims 4-6 and 14 are rejected under 35 USC 102(a) as allegedly being anticipated by Wong et al. (*Nano Lett.* (2002 June) 2, 583-587). The rejection states that Wong describes a process of preparing $SiO_2$/Au composites on the surface of nanoparticles. The rejection states that net positively charged peptide amphiphiles ($Lys_{200}Cys_{30}$) are mixed with a positively charged solution of Au salts. This solution is then mixed with a negatively charged solution $SiO_2$ solution. It is stated that the mineral Au ions inherently nucleate sites for formation of gold nanoparticles. Applicants respectfully traverse the rejection.

Applicants contend that the "peptide amphiphile" of Wong et al. is not within the meaning described in the instant application. Specifically, paragraph [0032] describes peptide amphiphiles within the scope of the invention as the following:

> [0032] Notwithstanding embodiments provided above, broader aspects of the present invention include a peptide amphiphile composition having a hydrophobic or lyophobic component and a lyophilic peptide or peptide-like component. In various preferred embodiments, the hydrophobic component of such a composition is of sufficient length to provide amphiphilic behavior and micelle formation in water or another polar solvent system. Typically, such a

> component is a $C_6$ or greater hydrocarbon moiety, although other hydrophobic, hydrocarbon and/or alkyl components could be used as would be well-known to those skilled in the art to provide similar functional effect. . . .

Moreover, Applicants have amended independent claim 4 to recite that the peptide amphiphile comprises a $C_6$ or greater hydrocarbon component and a lyophilic peptide component. Wong et al., on the other hand, describes the diblock copolypeptide, $Lys_{200}Cys_{30}$, as having amphiphilic properties, but these polypeptides do not meet the claim-recited definition of "peptide amphiphiles." Rather, these diblock copolypeptides lack a hydrocarbon component of $C_6$ or greater. Furthermore, Applicants have amended the claims to further clarify that the nanofibers are fibrous cylindrical micelles formed from the peptide amphiphiles.

The Advisory Action mailed 17 March 2008 contends that Figure 1 of the Wong reference describes a peptide amphiphile comprising a hydrocarbon moiety "$BrH_3N$-$(H_2C)_5$-" wherein "$(H_2C)_5$" is the "hydrocarbon component. However, Applicants have amended the claim to require that the hydrocarbon component have 6 or more carbons.

Furthermore, the Advisory Action states that Wong describes the self-assembly of nanorods, which, according to the Examiner, are equivalent to the instant cylindrical micelles. Applicants dispute this contention. Wong et al. use a diblock polypeptide (Lys)x-(Cys)y to form round, hollow spheres that are then used to bind pre-formed gold and silica nanoparticles from a sol suspension. Furthermore, on page 586 (bottom of first column), the authors state that by using different block lengths they can produce other shapes, such as "crumpled raisin-like shapes". The legend of Figure 4 even provides a "phase diagram" where they describe the shape of the assembly produced for different x and y of the (Lys)x-(Cys)y diblock polypeptide. The diagram presents three possibilities: S = sphere, R = raisin, F = film. Not only does this demonstrate that the Wong molecules could not be expected to form "fibrous cylindrical micelles", but it would seem to implicitly exclude that possibility.

Furthermore, the Advisory Action contends that the Wong reference describes self-assembled nanoparticles, which can form "Ag nanorods." Specifically, at page 586, second column, Wong states that "We found that n-Ag of various sizes and shapes, including Ag nanorods, also led to the formation of hollow spheres." Therefore, Wong is

not teaching that nanorods are being formed from the peptide assembly, but that one component of the hollow spheres, specifically, the silver particles, may be in the form of nanorods. As such, the conclusion that the "nanorods" of Wong et al. are equivalent to the claim-designated "cylindrical micelles" is clearly incorrect.

Furthermore, Claim 4 provides the combination of combining solutions having ions of a mineral salt with opposite charges, ***wherein minerals nucleate at the nanofiber's surface***. Applicants respectfully submit that Wong does not describe the presence of ions of mineral salts. There are silica ($SiO_2$) nanoparticles (termed n-Si Wong), which have a partial negative electrostatic charge on their surface, but they are not a salt ("salt" being defined as the product formed from the neutralization reaction of acids and bases), and are not an ion in solution ("ion" being defined as a atom or molecule having an ionic charge). There are also gold nanoparticles (termed n-Ag by Wong), but these are a metal with oxidation state Au(0). They are not a salt, do not have a net ionic charge (either the same or opposite the peptide) and, in fact, interact with the peptide through the gold-thiol bond with cysteine. Therefore, the presence of ions of mineral salts is not described in Wong.

Furthermore, Wong uses nanoparticles (n-Si and n-Au) that are separately pre-formed (having diameters of 10-12 nm and containing hundreds of atoms) and merely "stick" to the (Lys)x-(Cys)y diblock polypeptide assembly. In contrast, the instant application describes nucleation of minerals from ionic (salt) solutions (of individual atoms) at the surface of the peptide amphiphile assembly, which is a different process of mineral formation.

In conclusion, Wong does not anticipate the claims as amended. Withdrawal of the rejection is respectfully requested.

*35 USC 102 – Slocik et al.*

Claims 4-6 are rejected under 35 USC 102(a) as allegedly being anticipated by Slocik et al.

It is stated that Slocik describes the preparation of nanomaterials comprising histidine-rich self-assembled amphiphilic peptides (HREs) and metal sulfide composites,

where HREs stabilize nanoclusters. It is stated that positively charged peptides are mixed with positively charged silver nitrate solution. Then a second solution of $Na_2S$ is added to the first solution to produce $Ag_2S$/HREs nanofibers. Applicants respectfully traverse the rejection.

Applicants submit that "peptide amphiphiles" according to the present invention are not employed in the Slocik methods. To clarify, the claims have been amended requiring that a peptide amphiphile having a hydrocarbon component of 6 or greater carbons and a lyophilic peptide component be used in the claimed method. The Slocik reference, on the other hand, states that "[i]n the first step, metal-HRE complexes were formed by the 1:1 reaction of appropriate metal ion to peptide in a deaerated solution of Tris buffer . . ." (Slocik, page 170, col. 1.) Furthermore, Slocik describes the peptide used as AHHAHHAAD. (*Id.*) Therefore, this reference does not, in fact, teach the use of peptide amphiphiles, as defined in the claims and the present application. Furthermore, Applicants have clarified that the nanofibers made using the self-assembling peptide amphiphiles are fibrous cylindrical micelles. Each and every element of the claims has not been met. Accordingly, withdrawal of the rejection is respectfully requested.

***CONCLUSION***

Applicants believe that this amendment overcomes the outstanding rejections. Applicants, however, invite the Examiner to call the undersigned to discuss any remaining issues to expedite the prosecution of this application.

Respectfully submitted,

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